## Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 119-131 are pending in this application and are rejected on various grounds. Claims 119-123 have been amended with a functional recitation: "wherein said polypeptide induces proliferation of stimulated T lymphocytes in a mixed lymphocyte reaction". Further, all pending claims have been amended to remove references to "Figures". Claim 128 has been canceled without prejudice or disclaimer. The rejections to the presently pending claims are respectfully traversed.

## Priority

Applicants rely on the 'Mixed lymphocyte reaction' assay for patentable utility in this case, first disclosed in US Provisional Application 60/144758, filed July 20, 1999, priority for which has been claimed in this application. Applicants further submit that the subject matter defined in this application provides a specific and substantial asserted utility or a well established utility for the claimed invention for the same reasons as those discussed below under the utility section for the present application. Hence, the present application is at least entitled to an effective filing date of **July 20, 1999.**

## Specification

The disclosure has been amended to delete all "embedded hyperlink and/or other form of browser-executable code." Accordingly, Applicants believe that all objections to the specification have been overcome.

## Information disclosure Statement

The Examiner had objected to the previously submitted IDS because it did not comply with the requirements of 37 C.F.R. § 1.98(a)(2). Applicants hereby submit a new IDS separately enlisting each accession number for the sequence, the reference and the database where the sequence is available, from the previously filed Blast report of 5/31/2002 which complies with 37 C.F.R. § 1.98(a)(2). Consideration of this Information Disclosure Statement is respectfully requested.

**Claim Rejections – 35 USC § 101 and § 112, first paragaraph**

A. Claims 119-131 are rejected under 35 U.S.C. §101 allegedly because "the because the claimed invention is not supported by a specific, substantial and credible asserted utility or well established utility."

B. Claims 119-131 were rejected under 35 U.S.C. §112, first paragraph allegedly "since the claimed invention is not supported by either a substantially asserted utility or a well established utility, one skilled in the art clearly would not know how to use the claimed invention."

The Examiner asserts that the ability of a protein to stimulate lymphocyte proliferation does not support a specific and substantial utility for the claimed invention because allegedly the MLR assay is an artificial *in vitro* system that does not provide for specific conditions or diseases for which the claimed invention would predictably function. The Examiner adds that, the MLR assay is a measure of alloreactivity of one individual to another individual, rather than a general measure of immune function. Further, the Examiner asserts that the instant specification fails to provide sufficient detail of the (MLR) assay and fails to provide any data whatsoever in order for one of ordinary skill in the art to evaluate the conclusion that lymphocyte proliferation was stimulated by the claimed invention. For the reasons outlined below, Applicants respectfully disagree.

**Utility Standard**

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the

"substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance with the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: **"If the (A)pplicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."**

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the Applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

To overcome the presumption of truth based on an assertion of utility by the Applicant, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. **Absolute predictability is not a requirement.** Only after the Examiner has made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence.

Further, the legal standard with respect to *in vitro* or animal model data providing pharmacological activity has been commented on in *Cross v. Iizuka*, 753 F.2nd 1040, 1051, 224 USPQ 739, 747-48 (Fed. Cir. 1985):

> "We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the

compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vitro* utility."

Furthermore, M.P.E.P. 2107.03 (III) states that:

"If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process."

Thus, the legal standard accepts that *in vitro* or animal model data is acceptable utility as long as the data is "reasonably correlated" to the pharmacological utility described.

**Arguments**

Claim 128 has been canceled. Applicants respectfully disagree with and traverse the rejection to the remaining claims.

Without acquiescing to the propriety of this rejection, solely in the interest of expediting prosecution in this case, Applicants submit a declaration and supportive references from the art to support the immunostimulant activity of PRO1375.

Applicants submit a declaration by Sherman Fong, Ph.D. of Genentech, Inc., an expert in the field of Immunology and co-inventor of the present application, to show that there are specific immune stimulant utilities for compounds identified by an MLR assay. The Declaration explains how the MLR reaction was performed in the instant application using peripheral blood mononuclear cells (PBMCs), which contain responder T-cells, and allogenic, pre-treated (irradiated) PBMCs, which predominantly contained dendritic cells. As Dr. Fong emphasizes, immunostimulants are important and are very desirable in the treatment of cancer and in enhancing the effectiveness of previously identified treatments for cancer. Supportive evidence for this utility also comes from teachings in the art like Steinman *et al.* (Exhibit B) and Peterson *et al.* (Exhibit D). Steinman *et al.* state that "...**medicine needs therapies that enhance immunity or resistance to infections and tumors**. (page 1, column 1, line 7; emphasis added)". Peterson *et al.* (Exhibit D) show that, recently, the immune stimulant IL-12 was successfully

used in a cancer vaccine trial to treat melanoma. Further, as Dr. Fong explains regarding the IL-12 melanoma trial:

> "Due to the immune stimulatory effect of IL-12, **the treatment provided superior results** in comparison to earlier work, where the patients' own dendritic cells were prepared from peripheral blood mononuclear cells (PBMCs) treated with antigens, then cultured *in vitro* and returned to the patient to stimulate anti-cancer response" (Emphasis added).

Further, Dr. Fong's declaration clearly states that:

> "A PRO polypeptide shown to stimulate T-cell proliferation in the MLR assay of the present invention with an activity of at least 180% of the control is expected to have the type of activity exhibited by IL-12 and would find practical utility as an immune stimulant".

Similarly, as would be readily recognized by one skilled in the art based on the instant specification, the positive results obtained in the MLR assay for PRO1375 and the supportive examples in the art, the MLR assay results clearly establish utility for the polypeptides as immunostimulants. The specification, in turn, enables one skilled in the art to use the compounds for the asserted purpose. Thus, besides the immunostimulatory uses of PRO1375 polypeptides, for example, in the treatment of viral infections like HIV or Epstein Barr viral infections, Applicants assert specific utilities in the treatment of cancers like melanoma.

Further, since the legal standard accepts *in vitro* assays as acceptable utility and the data is "reasonably correlated" to the pharmacological utility based on the discussions above, a valid case for utility has been made and would be considered credible by a person of ordinary skill in the art for the PRO1375 polypeptides.

Thus, Applicants believe they have established patentable utility for PRO1375 claimed in the present application and this rejection should be withdrawn.

**Claim Rejections - 35 USC § 112, first paragraph -written description**

Claims 119-131 are rejected under 35 U.S.C. 112, first paragraph because allegedly, the subject matter was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing.

Specific utility has been asserted in the present invention based on MLR activity of PRO1375 and the pending claims recite this functional feature for the PRO1375 polypeptides. The pending claims are drawn to a genus of polypeptides defined both by sequence and functional identity. It would have been obvious to one skilled in the art at the effective priority date, in view of Applicant's possession of the PRO1375 sequence (SEQ ID NO:418), that the Applicant possessed obvious variations and adaptations of SEQ ID NO:418 as well, at the time of filing.

Hence, Applicants request that the present rejection to the present claims be reconsidered and withdrawn.

**Claim Rejections - 35 USC § 112, first paragraph -enablement**

Claims 119-131 are rejected under 35 U.S.C. §112, first paragraph for lack of enablement. The Examiner required that the cDNA deposited under ATCC accession number 203115 be required for practicing the claimed invention or be obtainable by a repeatable method set forth in the specification.

Applicants submit that amendments to the specification have (1) the current ATCC address; and (2) incorporated the requisite assurances specifying that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent." Thus, the CDNA would be available in a repeatable manner and this rejection should be withdrawn.

**Claim Rejections – 35 USC § 102**

a. Claims 119-125, 129-131 are rejected under 35 U.S.C. §102(b) as being anticipated by WO00/18904, dated June/2000; WO99/63088, dated September/1999; WO00/00610, dated June/2000; WO00/00506, dated June/2000.

b. Claims 119-125 and 129 are rejected under 35 U.S.C. §102(a) as being anticipated by EP1130094, dated September/2001.

Based on the discussions above, Applicants believe that they are entitled to at least an effective date of **July 20, 1999** for this application. Accordingly, none of the above cited references are prior art and these rejections should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C45). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: August 5, 2004

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